REMARKS

Claims 38-99 were pending in the application. Claims 38-99 have been canceled. New claims 100-118 have been added. Accordingly, upon entry of the amendments presented herein, claims 100-118 will remain pending in the application.

Support for new claims

No new matter has been added. Support for the amendments to the claims and specification can be found in the claims and throughout the specification as originally filed. Specifically, with respect to new independent claims 100 and 101, support for recitation of the phrase "topically applying for at least 30 days" can be found at least in Example 2 at page 48, lines 23-25 of the specification. Support for recitation of the phrase "1 to 15% w/w composition of Coenzyme Q10" can be found at least at page 6, lines 27-29 of the specification. Support for recitation of the phrase "topically applying....to the site of the melanoma" can be found at least at page 48, lines 20-25 and at page 33, lines 7-10 of the specification. Support for recitation of the phrase "effective to reduce the growth of the melanoma" can be found at least at page 33, lines 7-10; page 6, lines 23-24; page 7, lines 18-25; page 12, lines 14-17; and page 16, lines 3-7 of the specification. Support for recitation of the phrase "in an amount of no more than 4.0 mg per kg of body weight" can be found at least at page 32, lines 16-17 of the specification. With respect to dependent claims 105 and 106, support for recitation of the phrases "1 to 10% w/w composition of Coenzyme Q10" and "1 to 5% w/w composition of Coenzyme Q10" can be found at least at page 6, lines 27-29 and page 38, lines 9-11 of the specification. Support for dependent claims 102-104 and 107-118 find support at least in previously pending claims 40-42 and 60-72 and, more specifically, support as was previously provided by Applicants in the Second Preliminary Amendment filed on February 18, 2011 for previously pending claims 40-42 and 60-72 (*e.g.*, at least in Example 3 at pages 48-49 and Figures 11-14; in Example 1 at pages 42-48 and, in particular, at page 42, line 15 through page 43, line 10; Example 4 at page 49; and in Figures 1-5 of the specification).

As set forth in detail above, and as discussed during the numerous telephonic interviews with the Examiner, the claims provided herein are fully supported by the present specification

and are in compliance with the written description requirement (see, *e.g.*, *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976) and MPEP 2163.05).

Amendments to and cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and were done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Interview Summary

Applicants gratefully acknowledge the several telephonic interviews between Examiner Underdahl and Applicants' attorneys, including the most recent telephonic interview on June 22, 2011. During these telephonic interviews, an agreement was reached that unexpected results are provided in Example 2 and Figure 14 of the specification. Further, during these telephonic interviews, various versions of the claims provided herein were discussed.

Newly Presented Claims

The newly presented claims are directed to methods of treating melanoma in a subject that require topical application of a composition comprising Coenzyme Q10. Applicants respectfully submit that the newly presented claims are commensurate in scope with the unexpected results provided at least in Example 2 and Figure 14 of Applicants' specification.

Specifically, new independent claim 100 is directed to "a method of treating melanoma in a subject, comprising ***topically applying*** for ***at least 30 days*** a 1 to 15% w/w composition of Coenzyme Q10 ***to the site of the melanoma*** effective to ***reduce the growth of the melanoma***. New claim 101 further requires that Coenzyme Q10 is topically applied ***in an amount of no more than 4 mg per kg of body weight***.

Applicants respectfully submit that one of ordinary skill in the art would be able to practice the claimed methods by using no more than routine experimentation. Specifically, the ordinarily skilled artisan would have understood how to perform the methods presently being claimed after a reading of the specification, including Example 2 of the specification, combined with the common knowledge in the art at the time of the invention, *e.g.*, the common understanding of how a topical medication is applied to a skin condition. For example, the

ordinarily skilled artisan would have known (after reading at least Example 2 of the specification) to topically apply an amount of a composition comprising 1 to 15% w/w of Coenzyme Q10 directly to the site of a melanoma in a manner similar to, for example, applying an anti-acne medication to the site of a blemish or bacitracin to the site of a cut, by spreading a layer of the topical composition on the site of the melanoma to sufficiently cover the area being treated. The precise amount that is applied topically each day for the thirty days is therefore not critical to the efficacy of the composition.

Moreover, one of ordinary skill in the art would easily recognize the point at which the growth of a melanoma is reduced based on the teachings in the specification and the common knowledge in the art at the time of the invention. Specifically, one of skill in the art would know to: (i) take a baseline measurement of the melanoma (*e.g.*, the mass of the melanoma or size of the melanoma) prior to topical administration of the composition: (ii) topically apply the 1 to 15% w/w composition of Coenzyme Q10 to the site of the melanoma for at least 30 days; (iii) monitor the growth of the melanoma (*e.g.*, by monitoring the mass of the melanoma or size of the melanoma) at various times during and/or after 30 days of treatment; and (iv) determine if the melanoma (*e.g.*, the mass of the melanoma or size of the melanoma) had remained unchanged or decreased during and/or after 30 days of treatment. One of skill in the art would have had knowledge of the techniques required to monitor the growth of the melanoma based on the teachings in the specification and the common knowledge in the art. For example, the specification teaches at page 8, lines 18-20 that "[w]hen referring to a type of cancer that normally manifests as a solid tumor, a "clinically detectable" tumor is one that is detectable *on the basis of tumor mass; e.g., by procedures such as CAT scan, MR imaging, X-ray, ultrasound or palpitation…* ." Methods for monitoring the growth of a tumor were also commonly known and routine techniques in the art at the time of the invention.

In view of the foregoing, it is evident that the amount of direction and guidance disclosed in the specification, as well as the general knowledge in the art at the time of the invention, is sufficient to enable the skilled artisan to carry out the claimed methods using only routine experimentation. Accordingly, Applicants submit that the claims provided herein comply with the enablement requirement.

Allowed Claims to Methods of Treatment of Cancer

Applicants respectfully wish to point the Examiner's attention to granted claims in various U.S. patents in support of Applicants' position that one of ordinary skill in the art would know how to apply a topical composition for the treatment of a tumor and determine if the treatment was effective to reduce the rate of growth of the tumor and, therefore, that the claims provided herein are enabled. As the claims highlighted below are granted, they are presumed to be meet the requirements for both written description and enablement.

For example, claim 1 of U.S. Patent No. 7,879,823 is directed to a "method of ***slowing the progression of a cutaneous tumor*** comprising ***topical*** application of at least one composition containing a non-denatured, soy product in an amount of from about 0.01-99% by weight in a carrier, wherein said non-denatured, soy product comprises a non-denatured, Kunitz-type soybean trypsin inhibitor." Example 1 of U.S. Patent No. 7,879,823 demonstrates that administration of non-heat treated soymilk "had a dramatic effect on tumor volume" whereas "heated soymilk did not affect the rate of increase in tumor volume" (column 14, lines 36-41). Similar to the claims presented herein, claim 1 requires the soy product to be present within a range of specific percentages by weight in the composition. ***No specific dosage amounts are required by the claims***.

U.S. Patent No. 6,469,061 contains claim 12 directed to a "method for ***treatment of non-prostate cancer*** in mammals comprising administering a pharmaceutical composition containing as an active ingredient a therapeutically effective amount of a jasomate compound" having a particular structure. Claim 22 further requires "formulating said composition as for topical administration and ***topically*** applying said topical formulated composition into direct contact with a cancer in said mammal." ***No specific dosage amounts are required by the claims***.

US Patent No. 7,776,894 contains claim 1 directed to a "method for ***inhibiting melanoma*** growth, comprising contacting the melanoma with an effective amount of a celastrol derivative…", wherein the celastrol derivative has a specific structure. Similarly, claim 5 is directed to a "method for ***inhibiting melanoma metastasis,*** comprising contacting the melanoma with an effective amount of a celastrol derivative…", claim 7 is directed to a "method for ***sensitizing melanoma cells to apoptosis,*** comprising contacting the melanoma cells with an effective amount of a celastrol derivative…", and claim 9 is directed to a "method for ***treating***

melanoma in a subject in need thereof, comprising administering an effective amount of a celastrol derivative…", wherein the celastrol derivative has a specific structure. Dependent claims require that the composition is administered ***topically*** (claims 3 and 10). ***No specific dosage amounts are provided in the claims***.

U.S. Patent No. 7,824,673 contains claim 1 directed to a "***method for reducing the amount of adipose tissue*** at a selected location" by "introducing effective amounts of purified collagenase… wherein said adipose tissue is a lipoma." ***No specific dosage amounts are provided in the independent claim 1.***

In view of all of the foregoing, it is evident that a precise dose amount is not required for enablement of a claim directed to a method of treatment, *e.g.*, of a melanoma, non-prostate cancer or a cutaneous tumor, by administering, *e.g.*, topically applying, a composition or compound. Indeed, the ordinary skilled artisan would understand, based at least upon the common knowledge in the art, how to topically apply a composition to a site of a tumor and, moreover, would recognize when growth of a cancer was reduced or inhibited.

Request For Specific Reasons

If the newly presented claims are not held allowable, it is respectfully requested that specific reasons be provided as to why the ordinarily skilled artisan would not have known how to spread a topical composition over a melanoma site based on the teachings in the specification, *e.g.*, Example 2 of the specification. In particular, it is requested that specific reasons be provided as to why the ordinarily skilled artisan would not have known to simply spread a layer of the topical composition comprising Coenzyme Q10 as described in Example 2 so as to cover the melanoma site in a manner similar to putting acne cream on a blemish or bacitracin on a cut.

CONCLUSION

Applicants submit that the pending claims are in condition for allowance. If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' attorney at (617) 449-6500.

Applicants believe no fees are due with the filing of this preliminary amendment. The Director, however, is authorized to charge any fees due to our Deposit Account No. 50-4876, from which the undersigned is authorized to draw under Order No. 117732-01601.

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Respectfully submitted,

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